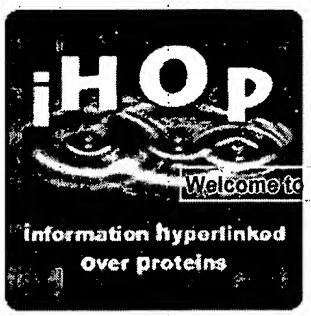
WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Monday, May 08, 2006

Hide?	Set Name	Query	Hit Count
	DB=USPT; PLUR=YES; OP=OR		
☐	L9	(6534635[PN])	1
☐	L8	(56534635[PN])	0
☐	L7	(5643752[PN])	1
☐	L6	(6812339[PN])	1
	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=OR		
☐	L5	L4 AND (TIMP1 OR TIMP$1)[CLM]	68
☐	L4	(TIMP1 or TIMP$1) AND colon AND cancer AND serum AND antibody	1412
☐	L3	L2 AND antibody	88
☐	L2	TIMP1 AND colon AND cancer AND serum	93
☐	L1	Tissue ADJ inhibitor ADJ of ADJ metalloproteinases AND colon AND serum	0

END OF SEARCH HISTORY



Symbol	Name	Synonyms	Organism
TIMP1	TIMP metallopeptidase inhibitor 1	CLGI, Collagenase inhibitor, EPA, EPO, Erythroid potentiating activity, Fibroblast collagenase inhibitor, HCI, Metalloproteinase inhibitor 1 precursor, TIMP, TIMP-1, tissue inhibitor of metalloproteinase 1 (erythroid potentiating activity, collagenase inhibitor), Tissue inhibitor of metalloproteinases	Homo sapiens

Search
Gene

Show overview new
Find in this Page

Filter and options

Gene Model
Help

UniProt	P01033, Q9UCU1, Q14252
PDB Structure	1LQN, 1UEA
OMIM	305370
NCBI Gene	7076
NCBI RefSeq	NP_003245
NCBI RefSeq	NM_003254
NCBI UniGene	7076
NCBI Accession	BAA01913, AAA63234

Interaction information for this gene ...

Enhanced PubMed/Google query ... new

WARNING: Please keep in mind that gene detection is done automatically and can exhibit a certain error. Read more about synonym ambiguity and the iHOP confidence value ☆☆☆.

Find in this Page

MMP and TIMP [?] ☆ protein expression was measured by single or double labelled immunohistochemistry, and mRNA expression by in situ hybridisation.

Change of TIMP-1 [?] ☆ mRNA expression in adeno-epithelial and mesenchym before and after treatment was insignificant (0.588 +/- 0.191 vs 0.621 +/- 0.146, P < 0.05).

Leptin stimulated TIMP-1 [?] ☆ protein, mRNA, and promoter activity.

CONCLUSIONS: Tenon fibroblasts contain the ability on the mRNA level to synthesize all enzymes of the MMP and TIMP [?] ☆ family that are related to remodeling of the extracellular matrix.

TIMP-1 [?] ☆ and -2 mRNA transcripts were evaluated by RT-PCR.

In the present study, to evaluate the potential roles of matrix degrading proteases in luteal development and regression, we examined gelatinases and TIMP-1 ☆, -2, -3 mRNA expressions, as well as gelatinase activity in rat CL during pregnancy and postpartum using Northern blot, in situ hybridization, and gelatin zymography, respectively.

Concept & Implementation

by Robert Hoffmann

We show that treatment of TSU-Pr1 cells with **staurosporine** results in induction of **TIMP-1 [?]** **mRNA** and protein secretion.

We are the first to report that **mRNA** expression and protein secretion of **TIMP-1 [?]** are enhanced by **staurosporine** treatment in **prostate cancer** cells.

We conclude that DLPC prevents TGF-beta1-mediated HSC fibrogenesis through down-regulation of alpha1(I) **procollagen** and **TIMP-1 [?]** **mRNA** expression.

In this study, we have undertaken a detailed analysis of expression of the **TIMP [?]** family in normal human brain and **malignant gliomas** at both the **mRNA** and protein level.

MMP and **TIMP** **mRNA** was quantified through use of competitive RT-PCR, and protein was detected by means of **Western blotting** and **ELISA**.

It had no significant effect on the production and expression of **TIMP-1 [?]** **mRNA** in **chondrocytes**.

RESULTS: The expression of **messenger RNA** (**mRNA**) for **collagen** III and **TIMP-1 [?]** was significantly higher in patients receiving **cyclosporin** therapy than in those having **tacrolimus** ($P < 0.01$); this finding was accounted for by differences in the biopsy material at 1 week.

There were no significant differences of pro-(alpha1)-collagen-I, (alpha2)-collagen-IV, and alpha-smooth muscle **actin** (alpha-SMA) **mRNA** expression in the **liver** between TIMP-Tg and Cont-mice, suggesting that overexpression of **TIMP-1 [?]** itself did not cause hepatic stellate cell (HSC) activation.

In addition, the tumors with positive estrogen or **progesterone receptors** showed a higher **TIMP-1 [?]** **mRNA** expression than those without the receptors, but this did not reach statistical significance.

TIMP-1 [?] **mRNA** was up-regulated by **cyclosporine** in **fibroblasts**.

MMP and **TIMP** **mRNA** and protein expression levels were also studied in s.c. **xenograft** lesions derived from a selection of these cell lines.

METHODS: Surgically removed subfoveal fibrovascular **membranes** from five eyes were analyzed for the expression of MMP and **TIMP [?]** **mRNA**.

During late fetal development, MMP-1 **mRNA** expression in both cell types increases close to term (day 21, term = 22 days), while that of **stromelysin** and **TIMP-1 [?]** remain constant.

top

The inhibitor **TIMP-1 [?]** **mRNA** was first detected 6 hours after **injury** and showed a marked peak of expression at 24 hours; however, no expression was detected by 7 days.

In situ hybridization localized **TIMP-1 [?]** **mRNA** to the **corpus luteum** at D18 and PP1, and to oocytes at specific stages of follicular development.

This study was designed to assess whether the glomerular expression of **mRNA** for extracellular matrix (ECM) components including alpha 1 (I), alpha 1 (III), and alpha 1 (IV) collagen chains, laminin B1 and B2 chains, metalloproteinases (MMP), and tissue inhibitor of metalloproteinases (**TIMP**) is affected by **enalapril** in 12- and 24-wk-

old rat after streptozotocin injection.

The present study was designed to assess whether expression of **mRNA** for extracellular matrix (ECM) components, metalloproteinases (MMP) and **tissue inhibitor of metalloproteinases** (**TIMP [?]**) in glomeruli is affected by a low protein diet during the course of **focal glomerulosclerosis** (FGS).

The expression of **collagenases** and **TIMP-1 [?]** was examined immunohistochemically in 50 cases of surgically obtained specimens of primary LSCCs.

Additionally, ET-1-induced **collagenase** activity, **type II collagen** metabolites, and tissue inhibitor of metalloproteases 1 (**TIMP-1**) protein were evaluated.

This effect is not only produced by a stimulation of matrix protein formation: a complex regulation of MMP and **TIMP [?]** interaction, namely decrease of expression and activity of interstitial **collagenase** and an enhanced inhibition by increased levels of TIMPs, are involved.

Furthermore, alpha-tocopherol, which inhibits **protein kinase C** activity, is able to diminish **collagenase** gene transcription without altering the level of its natural inhibitor, tissue inhibitor of metalloproteinase, **TIMP-1 [?]**.

TIMP-1 [?] and -2 protein amounts in GCF were measured by **ELISA**, and active and APMA-activatable **collagenase** activities were determined by functional assays using image-analysis after **SDS-PAGE**.

From the tissue extract, proteins were separated on a gel-filtration column (Sephacryl S-200) and analysed for MMP and **TIMP** activity by zymography as well as by using succinyl-Gly-Pro-Leu-Gly-Pro-4-amido-7-methyl coumarin (Suc-GPLGP-AMC) as a selective **fluorogenic substrate** for **collagenase**.

Interferon-gamma up-regulated **TIMP-1** production by MEC and blocked PMA and TNF-induced up-regulation of **collagenase**.

All-trans **retinoic acid** (RA) decreased **collagenase** expression and stimulated **TIMP-1** expression.

Anti-CD3-activated T cell **clones** stimulated the production of **collagenase** both in THP-1 cells and **fibroblasts**, whereas **TIMP** levels were not influenced.

Our data collectively indicate that activated **T cells** in contact with monocytic cells or **fibroblasts** may alter the balance between interstitial **collagenase** and its specific inhibitor **TIMP**.

Collagenase activity and serine proteases (elastase-like, cathepsin G-like and trypsin-like activities) of **saliva** (n = 10) and gelatinase, lactoferrin and **TIMP-1** of **saliva** (n = 10) and serum (n = 10) samples before and after 2 months **doxycycline** treatment, combined with NSAID, were studied by quantitative **SDS-PAGE** assay, **ELISA** assay and by spectrophotometric assay.

CONCLUSIONS--Fibroblast, but not neutrophil type, **collagenase** is synthesised, secreted, and subsequently activated, but is not inhibited by **TIMP [?]** in labial **salivary glands** or **saliva** in SS.

OBJECTIVE: To profile the expression of all known members of the matrix metalloproteinase (MMP), ADAMTS, and **tissue inhibitor of metalloproteinases** (**TIMP [?]**) gene families in normal **cartilage** and **cartilage** from patients with osteoarthritis (OA).

To examine matrix metalloproteinase (MMP) and **tissue inhibitor of metalloproteinases** (**TIMP [?]**) mRNA levels in archival **breast**

cancer biopsies, we employed microdissection to separate tumour tissue from the surrounding breast tissue, or stroma and RT-PCR to determine gross qualitative and small quantitative differences in the patterns of expression.

OBJECTIVES: To investigate the secretion profiles of matrix metalloproteinases (MMP) and their inhibitors (TIMP) in synovial fluid-derived fibroblasts and to compare them with those of tissue-derived fibroblasts.

Deficient migration by specific lines of aged fibroblasts was not related to the capacity to attach, express alpha2 integrin, or secrete MMPs and TIMP1, but was characterized by disorganized cytoskeletal actin and reduced alpha2beta1 function.

top

In KE-3 esophageal cancer cells and SW620 colon cancer cells, both the binding activity of CRTF and TIMP-1 [?] concentration increased in the presence of a conditioned medium (CM) of fibroblasts which was isolated from human colon cancer tissues, but did not increase in MKN-45 cells.

OBJECTIVE: To determine the effects of calcium pentosan polysulfate (CaPPS) on the production of matrix metalloproteinases (MMPs) and their endogenous inhibitors, tissue inhibitors of metalloproteinases (TIMP), in cultures of rheumatoid synovial fibroblasts.

OBJECTIVE: To determine whether, in human fibroblasts and chondrosarcoma cells, the regulation of interleukins (IL)-6, 8, and 11 and matrix metalloproteinases (MMP)-1, 3, and 13, and their tissue inhibitor TIMP-1, depends on the transcription factor nuclear factor-kappaB (NF-kappaB).

Cyclosporine treatment induces ECM accumulation by increasing collagen synthesis in endothelial and epithelial cells and reducing its degradation by up-regulating TIMP-1 [?] expression in fibroblasts.

The inhibitor of metalloproteinases, TIMP-1 [?], is mainly expressed in fetal lung fibroblasts.

To examine whether heparin and cholesterol induce MMP and tissue inhibitor of metalloproteinase (TIMP) in human heart fibroblast (HHF) cells, confluent HHF cells were treated with cholesterol (100 microM) or heparin (20 microM).

Cyclooxygenase inhibitors enhance the production of tissue inhibitor-1 of metalloproteinases (TIMP-1 [?]) and pro-matrix metalloproteinase 1 (proMMP-1) in human rheumatoid synovial fibroblasts.

RESULTS: RhIL-1 beta augments the production of TIMP-1 and proMMP-1 in synovial fibroblasts from RA patients, and this IL-1-induced production of TIMP-1 [?] and proMMP-1 was further enhanced by treatment with the cyclooxygenase inhibitors, indomethacin and diclofenac.

Stimulation of gelatinase B and tissue inhibitors of metalloproteinase (TIMP) production in co-culture of human osteosarcoma cells and human fibroblasts: gelatinase B production was stimulated via up-regulation of fibroblast growth factor (FGF) receptor.

The effects of ultraviolet A (UVA) radiation and reactive oxygen species (ROS), generated with a xanthine and xanthine oxidase (XOD) system, on collagen enzymatic degradation involving the matrix metalloproteinase (MMP) and its tissue inhibitor of metalloproteinase (TIMP) were investigated using cultured human dermal fibroblasts.

A panel of six **monoclonal antibodies** (MAbs) was raised against purified human **fibroblast** tissue inhibitor of metalloproteinase-1 (**TIMP-1**) and characterised.

Tropoelastin, **collagen** and fibrillin levels were stable between days 4 and 10, and MMP and **TIMP** decreased by day 10.

All diabetes-associated changes in MMP and **TIMP** mRNA and activities were attenuated by perindopril treatment in association with reduced type IV **collagen** accumulation.

Gene expression of matrix metalloproteinase (MMP) and tissue inhibitor of metalloproteinase (**TIMP**) was measured by **RT-PCR** and type IV **collagen** content by immunohistochemistry.

The reproductive hormone **relaxin** has been reported to reduce **collagen** and **TIMP-1** expression by dermal and lung fibroblasts and thus has potential antifibrotic activity in **liver fibrosis**.

Elevated serum levels of type I **collagen** degradation marker ICTP and tissue inhibitor of metalloproteinase (**TIMP**) 1 are associated with poor **prognosis** in **lung cancer**.

EXPERIMENTAL DESIGN: From the sera of 141 **lung cancer** patients, we assessed markers of type I **collagen** synthesis (PINP and PICP) and degradation (ICTP) by **radioimmunoassays**, and we assessed MMP-9 and its tissue inhibitor **TIMP-1 [?]** by **ELISA**.

Additionally, rapidlattice contraction and **collagen** degradation were blocked when **collagen** lattices were treated simultaneously with **plasmin** and **aprotinin** or a tissue inhibitor of metalloproteinases, **TIMP-1 [?]**.

Thus, in croton oil-induced rat pouch model, the subcutaneous accumulation of pouch tissue **hydroxyproline** over the course of 10 days is initially associated with a VA-positive myoFb phenotype and its transcription of TGF-beta1, type I **collagen** and **TIMP-1**.

In vitro studies also revealed upregulation of type IV **collagen** and **laminin** gene expression associated with the **hTIMP-1** overexpression.

top

Immunohistological examination revealed increased amounts of the **basement membrane** (BM) components, type IV **collagen** and **laminin**, in the **hTIMP-1** overexpressing tumors compared to that of the control.

Furthermore, exogenous TGF-beta1 (0 to 10 ng/ml) did not mimic **hypoxia**, as it stimulated MMP-2 activity and increased the expression of **collagen** IV, **collagen** I and **TIMP-1** mRNA.

Although **hypoxia** stimulated **TGF-beta** production (2- to 3-fold), neutralizing anti-TGF-beta1 antibody did not abolish the hypoxia-induced changes in **gelatinase** activity, **TIMP-1**, **collagen** IV or **collagen** I mRNA expression, implying that TGF-beta1 is not the mediator.

[Immunohistochemical localization of **matrix metalloproteinases** (MMP) and tissue inhibitors of metalloproteinases (**TIMP [?]**) in tuberculous pleuritis].

Matrix metalloproteinases (MMP) and tissue inhibitors of metalloproteinases (**TIMP [?]**) have been found by ELISA and gelatine zymography in different concentrations in pleural fluid in tuberculous (TB) pleuritis.

Our results suggest that serum **MMPs**, **TIMP-1** and proinflammatory

cytokines play an important role in the pathophysiology of the acute coronary syndromes.

When comparing the expression of cytokines, MMPs, and TIMP-1 [?] in PLS patients with clinically active and non-active periodontitis, the non-active PLS patients showed significantly higher values of IL-1beta than the patients with active periodontal disease (ANOVA, P < 0.01).

The aim of the present study was to compare concentrations of cytokines, matrix metalloproteinases (MMPs) and a metalloproteinase inhibitor (TIMP-1 [?]) in gingival crevicular fluids (GCF) from sites with gingival inflammation in 28 young patients with Papillon-Lef?vre syndrome (PLS), and in age- and gender-matched controls.

Elements of the nitric oxide pathway can degrade TIMP-1 [?] and increase gelatinase activity.

CONCLUSIONS: Our data show that peroxynitrite or nitric oxide can decrease TIMP-1 [?] and increase gelatinase activity, respectively.

Estrogen may improve the imbalance between the amounts of MMPs and TIMP in chondrocytes, and these results suggest that hormone replacement therapy may provide some chondroprotective effect.

The aim of this study was to examine differences in the patterns of metalloproteinases (MMPs) and MMP inhibitor (TIMP-1 [?]) expression in advanced human atheromas, both in relation to the plaque features and the vascular bed involved.

Here, we determine changes in the matrix metalloproteinases (MMP) and their tissue inhibitors (TIMP [?]) in relation to ECM production and the progression of renal fibrosis in subtotally nephrectomized (SNx) rats.

The serum concentrations of MMPs and TIMP-1 [?] clearly identified patients with two different histological types of rheumatoid synovitis and with OA.

These results show that both MMPs and TIMPs are produced by some astrocytes, but TIMP [?] production is particularly strong, especially in deep cortex and white matter which is more inhibitory for axon regeneration.

These alterations in MMPs and TIMP-1 [?] favor accumulation of extracellular matrix, structural components associated with bladder wall thickness and decreased compliance.

Therefore, using a novel device of our own design, we applied hydrostatic pressures in the physiological range to human bladder smooth muscle cells to determine the effect on MMPs, TIMP-1 [?] and transcription of the major structural collagens (types I and III).

There is no upregulation of MMPs or changes in TIMP expression in the nasal mucosa of patients with allergic rhinitis.

The effects of EST on the expression of matrix metalloproteinases (MMPs) and tissue inhibitor of metalloproteinase-1 (TIMP-1 [?]) in the transformed human chondrocyte cell line T/C28a4 were assessed by northern blot analysis.

AIM: To examine epiretinal membranes of proliferative diabetic retinopathy (PDR) for the presence of selective matrix metalloproteinases (MMPs) and their natural inhibitors (TIMPs), in order to determine whether neovascularisation and fibrosis, characteristic of this complication of diabetes mellitus, are associated with specific anomalies of MMP or TIMP [?] expression.

top

RESULTS: Invasiveness, **gelatinase** activity, and the expression of **TIMP-1 [?]** were higher in KLE cells than in Ishikawa cells, and they were increased by treatment with rTGF-beta 1.

There was little **gelatinase** or **TIMP [?]** activity in **amniotic fluid** in the first trimester.

Bullous keratopathy **corneas** showed **TIMP [?]** staining patterns similar to normal **corneas** and increased **gelatinase** A staining in regions of subepithelial fibrosis.

The spatial and temporal distribution of the **gelatinases** and **TIMP-1 [?]** suggests unique roles for these proteins in the rat **ovary**.

Divergent regulation of **gelatinase** and **TIMP** expression implies that either net synthesis or net degradation of basement membrane can be mediated by appropriate combinations of **growth factors** and **cytokines**.

We have examined the effects of **tumor necrosis factor alpha** (TNF) and **lymphotoxin** (LT) on **gelatinase** (72 kDa and 92 kDa) and tissue inhibitor of metalloprotease 1 (**TIMP1**) secretion by human myeloblastic leukemia cells (ML-1) in vitro.

Gelatinase B and **TIMP-1** were concomitantly overexpressed in primary **glioblastomas**.

Dexamethasone produces no significant change in **gelatinase** A and only small increases in **stromelysin**, **gelatinase** B, and **TIMP1**.

Interleukin-1 alpha produces a dose-dependent several-fold elevation of **gelatinase** B, **stromelysin**, and **TIMP1** without changing **gelatinase** A levels.

When added together, **dexamethasone** antagonizes the **interleukin-1** alpha-induced increase of **stromelysin**, **gelatinase** B, and **TIMP1** in a dose-dependent manner.

Tissue inhibitor of metalloproteinase 1 (**TIMP1**) is a contributory factor to fibrosis of a variety of organs including the **liver**.

UTE-1 is a regulatory **DNA** motif essential for **TIMP1** promoter activity in a variety of cell types including hepatic stellate cells (HSC), the key profibrogenic cells of the **liver**.

Analysis of MMP and **TIMP [?]** expression show that although most of these genes are not constitutively expressed in the normal **liver**, they are induced in a specific time-dependent manner following I/R.

In order to determine whether the expression of tissue inhibitors of metalloproteinases (TIMPs) reflects these changes and can be used as a marker for the activity of ongoing fibrosis, we studied **TIMP-1**, 2 and -3 in **liver** and serum/plasma of patients with **chronic hepatitis C**, hepatitis C virus-induced cirrhosis and healthy controls.

The cytokine-specific regulation of MMP/TIMP expression in hepatic stellate cells suggests that the initial matrix breakdown following **liver** injury might be enhanced by **TNF-alpha**, while diminished matrix degradation during chronic tissue injury might be due to the action of TGF-beta1 through **TIMP [?]** induction.

In this study, we therefore examined the in situ expression of immunoreactive MMP and tissue inhibitors of MMP (**TIMP**) in 10 normal **livers**, 11 surgically resected intrahepatic **cholangiocarcinomas** (CCs), and 6 surgically resected **hepatocellular carcinomas** (HCCs).

We investigated serum and **synovial fluid** (SF) concentrations of

MMP-3 and its tissue inhibitor (TIMP-1 [?]) in juvenile idiopathic arthritides (JIA).

METHODS: First, 1 x 10(9) plaque-forming units (pfu) of replication-deficient recombinant adenoviruses encoding either beta-galactosidase (ad beta gal), MMP-3 (AdMMP-3), or TIMP-1 [?] (AdTIMP-1) were added into the lumen of hSVGs for 1 hour.

We have developed quantitative assays for interstitial collagenase, stromelysin 1 and tissue inhibitors of metalloproteinase (TIMP [?]) 1 and 2, which have allowed the study of serum levels of these proteins.

Tear levels of pro-MMP-1, pro-MMP-9, and TIMP-1 [?] were measured by enzyme-linked immunosorbent assay (ELISA).

top

Results were compared with histology, hepatic expression of tissue inhibitor of metalloproteinases (TIMP)-1, -2 and -3, procollagen types I and IV, laminin, and with circulating protein levels of hyaluronate, TIMP-1 and -2 and MMP proenzymes, as measured by ELISA.

To measure quantitatively the expression of these MMPs and their endogenous inhibitors (TIMP-1 [?] and -2), we analysed samples from 52 patients with relapsing-remitting and primary progressive multiple sclerosis by ELISA (enzyme-linked immunosorbent assay) and substrate-gel electrophoresis (zymography).

TGF-beta did not regulate the expression of TIMP-1 [?] or -2 in either stromal or epithelial cells.

It is known that platelet derived growth factor (PDGF) and transforming growth factor-beta (TGF-beta) are involved in the regulation of MMP activity and tissue inhibitor of metalloproteinase (TIMP) production in non-ocular tissues.

Such a differential regulation of MMP and TIMP [?] by TGF-beta may influence the rate of extracellular matrix (ECM) turnover following tissue injury, induced during myomectomy and Caesarean section, or in leiomyomas during growth.

Synthesis of tissue inhibitor of metalloproteinase-1 (TIMP-1) in human hepatoma cells (HepG2). Up-regulation by interleukin-6 and transforming growth factor beta 1.

CONCLUSIONS: Helicobacter pylori infection results in a substantial increase in MMP-9 and MMP-2 activity in the gastric mucosa, probably contributed to in large part by tissue-resident macrophages, while no changes were seen in the TIMP levels.

CONCLUSIONS: Nitroglycerin in pharmacologically relevant concentrations activates MMP but represses TIMP [?] expression in human macrophages.

Plaques (n=24) contained abundant TIMP-1 [?], -2, and -3 in macrophages in plaque shoulders, intimal-medial borders, and areas overlying the lipid core, as well as in medial smooth muscle cells, albeit in lesser amounts.

Without any treatment, overexpression of TIMP-1 [?] itself did not induce liver fibrosis.

Fibrogenesis and fibrolysis in collagenous colitis. Patterns of procollagen types I and IV, matrix-metalloproteinase-1 and -13, and TIMP-1 [?] gene expression.

In situ hybridization localized TIMP-1 [?] to glial tumour cells and also to the surrounding tumour vasculature.

The elevated systemic TIMP-1 [?] concentration might contribute to

tissue **fibrosis**, leading to pathological **scar** formation.

By **Western blot** assay, **TIMP-1** and proMMP-1 were present and were expressed similarly in media from 2D versus 3D cultures, whereas active MMPs-1, -9, and -13 were not detected.

The relation of the expression of **TIMP-1 [?]** to the depth of invasion, lymph node **metastasis**, and TNM stage was negative(Pearson contingency coefficient were 0.1688, 0.3556, and 0.3004, respectively $P < 0.05$).

The imbalance between MMP and **TIMP** may be a critical factor which affects biologic behavior of **lung** carcinogenesis, invasion and **metastasis**.

TIMP-1 [?] overexpression in **pancreatic cancer** attenuates tumor growth, decreases implantation and **metastasis**, and inhibits angiogenesis.

This study was undertaken to determine the effects of overexpression of a natural tissue inhibitor of MMP (**TIMP-1 [?]**) on **pancreatic cancer** cell growth, **metastasis**, and angiogenesis.

Western blot analysis confirmed that BCP crystals down-regulate the synthesis of **TIMP-1 [?]** and -2.

In contrast to pathological **bone**, many osteoclasts were **TIMP-1 [?]** positive.

top

In contrast, the expression of **TIMP-1 [?]** varied markedly between the three types of **bone**.

In heterotopic **bone** only occasional low level **TIMP-1 [?]** expression was detected in **chondrocytes** and **osteoblasts**.

Osteophytic **bone** showed varying levels of **TIMP-1 [?]**, which was matrix-bound in fibrous tissue and cell-associated in **osteoblasts**, **chondrocytes**, and occasional mononuclear cells.

Neonatal **rib bone** showed consistent expression of **TIMP-1 [?]**, particularly in **chondrocytes**, **osteoblasts**, and lining cells.

Western blot analysis and **SDS-PAGE** substrate zymography were used to detect metalloenzymes and their natural inhibitor, tissue inhibitor of metalloproteinase (**TIMP-1**) in aqueous samples.

Modulation of matrix metalloproteinase and **TIMP-1 [?]** expression by **cytokines** in human RPE cells.

CONCLUSIONS: These data suggest that increased serum levels of **TIMP-1 [?]** and **cytokines** may reflect severe hepatic inflammation and that **plasma exchange** is an effective therapy to reduce these levels.

AIMS: The present study assessed whether the serum concentrations of tissue inhibitor of metalloproteinase 1 (**TIMP-1 [?]**) and **cytokines** are altered in patients with fulminant **hepatitis** and whether **plasma exchange** affects these concentrations.

The results suggest that OM as well as **IL-6** and LIF, other **cytokines** acting through similar receptor pathways, may act to inhibit net MMP activity by specifically up-regulating **TIMP-1** expression.

This study has evaluated the association of the expression levels of the **TIMP [?]** forms 1, 2, 3, and 4, measured by quantitative real-time RT-PCR, with classical clinicopathological characteristics, ie age, menopausal status, tumour size, histological grade, number of involved lymph nodes, and steroid hormone receptor status, and with disease progression and treatment sensitivity in 273 **breast cancer** patients.

This is the first study to report that pro-MMP-9 and TIMP-1 [?] serum concentrations are inversely correlated in breast cancer patients.

TIMP1 overexpression in cancer cells appears for the first time to be a promising indicator of favorable prognosis in breast cancer.

The present study examined whether changes in oxygen levels affect TIMP and MMP expression by cultured trophoblast and breast cancer cells.

CONCLUSION: This is the first comprehensive expression profile of all known MMP, ADAMTS, and TIMP [?] genes in cartilage.

CONCLUSION: Placental explants from IUGR pregnancies demonstrated reduced MMP-2, MMP-9, and TIMP-1 [?] release compared with explants from normal pregnancies at high (20%) but not low (3%) oxygen.

Finally, the addition of plasmin to the invasion assay using Matrigel resulted in an increase in invasiveness of HFH-T2 and HepG2-HBV cells, as well as MMP-9 activation, but the treatment with TIMP-1 [?] inhibited the invasiveness of HFH-T2 and HepG2-HBV cells as well as MMP-9 activation.

Increased TIMP [?] levels in arthritic cartilage may not be a sufficiently effective defense against cartilage resorption by excessive multiple MMPs and aggrecanases.

Thus, neutrophils contrast sharply with mononuclear leukocytes, which produce gelatinase A constitutively, synthesize gelatinase B de novo after adequate triggering, and overproduce TIMP-1 [?].

A 744-bp cDNA for TIMP-1 [?] including the entire coding sequence of 624 bases was cloned and sequenced.

Using this SSH approach, a cDNA that encodes tissue inhibitor of matrix metalloproteinase- (TIMP-1 [?]) was identified.

top

Degenerate PCR primers derived from highly conserved regions of TIMP family cDNAs amplified a 402-bp product from human fetal kidney cDNA.

Both 10 mM EDTA and 100 nM tissue inhibitor of metalloproteinase (TIMP [?]) significantly inhibited cartilage matrix degradation.

TIMP-1, -2, -3, and -4 in idiopathic pulmonary fibrosis. A prevailing nondegradative lung microenvironment?

Thus, the two main joint tissues, synovial membranes and cartilage, express TIMP genes.

There was a striking decrease in the amount of TIMP1 secreted by RASE compared with normal synovium.

TIMP-1 expression was demonstrated by Northern blot analysis in the multipotential neoplastic K-562 cell line, the high grade Burkitt's B-cell lymphoma lines, isolated tonsillar B cells and at low levels in peripheral blood T cells, but was not expressed in any of the neoplastic T-cell lines or isolated peripheral blood B cells.

TPA-sensitive MMPs and TIMP-1 were variably stimulated by biologically relevant cytokines, such as IL-1 and TNF-alpha.

Collagenase and stromelysin activities have been found to be overexpressed in skin cultures of some recessive dystrophic epidermolysis bullosa patients, and tissue destruction in the disease process might result from an imbalance of metalloproteinases (MMP) over tissueinhibitor of metalloproteinases (TIMP [?]).

Down-regulation of tissue inhibitor of matrix metalloprotease-1 (**TIMP-1 [?]**) in aged human **skin** contributes to matrix degradation and impaired cell growth and survival.

RESULTS: 4'-Hydroxy aceclofenac, a major metabolite of aceclofenac, down-regulated both basal and IL-1beta-induced production of proMMP-1 and proMMP-3 at a concentration sufficient to suppress **PGE2** production without modulating proMMP-2 or **TIMP-1 [?]**, whereas aceclofenac itself had no marked effect on the production of proMMPs.

METHODS: The amounts of **TIMP-1 [?]**, proMMP-1 and **PGE2** was measured by enzyme linked immunosorbent assay (ELISA).

Exogenous **PGE2** significantly suppresses **indomethacin**- and diclofenacenhanced **TIMP-1 [?]** and proMMP-1 production.

Addition of a vascularized skin **flap** may result in rapid remodelling of **granulation tissue** due to a decrease in expression of the trophic **growth factor** TGF-beta1 and increased degradation of extracellular matrix due to an alteration in the balance between MMPs and their inhibitor, **TIMP-1 [?]**.

CONCLUSION: The balance between the concentrations of stromelysin-1 and of **TIMP-1 [?]** in the **synovial fluid** appears to determine whether the progelatinase B molecule causes conversion into the active form.

The levels of both stromelysin-1 and **TIMP-1 [?]** were determined for each group and the concentration ratio of stromelysin-1/TIMP-1 in the **synovial fluids** of each group was highly correlated to the activation of progelatinase B.

TIMP-1 [?] was mainly present in the blood vessels and thecal cells, with minor staining in the **granulosa cells**.

Thus **TIMP-1** production by luteinized **granulosa cells** in culture is gonadotrophin dependent.

The capacity of **leptin** to induce **TIMP-1 [?]** and its signaling molecules were investigated in a human HSC **cell line**, LX-2.

OBJECTIVE: To study the effects of Anti-fibrosis Compound contained **serum** (AFCS) on **procollagen type I** and IV (ProC-I and ProC-IV), matrix metalloproteinase (MMP) and its tissue inhibitor (**TIMP-1 [?]**) gene expression in hepatic stellate **cell line** LI90 (HSC-LI90).

To characterize differences in **ear** wounding responses between regenerating and nonregenerating mice, we examined and compared the **extracellular matrix** remodeling and the matrix metalloproteinase (MMP) and tissue inhibitor of metalloproteinase (**TIMP**) response in the MRL and C57BL/6 mouse strains after injury.

top

Since all female **cell lines** examined showed methylation of the **TIMP1** promoter, the contribution of expression from the inactive X appears minimal.

BACKGROUND: The expression of tissue inhibitor of matrix metalloproteinase (**TIMP**) 1 in tumour tissue from patients with **colorectal carcinoma** has been reported to be related to disease progression.

CONCLUSION: These data suggest that the plasma concentration of **TIMP-1 [?]** correlates with both invasion and metastasis in patients with **colorectal carcinoma**.

Human **keratinocyte cell lines** differ in the expression of the

collagenolytic matrix metalloproteinases-1,-8, and -13 and of **TIMP-1 [?]**.

Simultaneous measurement of soluble **carcinoembryonic antigen** and the tissue inhibitor of metalloproteinase **TIMP1** serum levels for use as markers of pre-invasive to invasive **colorectal cancer**.

Our overall results indicate that simultaneous measurements of serum sCEA and **TIMP1** in patients with **colorectal cancer** could be used as prognostic and diagnostic markers for **disease progression** from the pre-invasive nodal phase to the invasive phase (stages I, II to III, IV).

Chemokine modulation of matrix metalloproteinase and **TIMP [?]** production in adult rat **brain microglia** and a human microglial **cell line** in vitro.

Tissue inhibitors of metalloproteinases (**TIMP**) block proteolytic degradation of **extracellular matrix** and consequently impede tumor invasion and metastasis.

The strong correlation between enhanced **extracellular matrix** gene expression, differential MMP and **TIMP [?]** gene expression, and histopathological evidence of fibrosis suggest that dysregulated matrix remodeling is likely to contribute to the pathology of bleomycin-induced **pulmonary fibrosis**.

Here we show that the same mutant inhibits apoptosis of human **breast epithelial cells**, suggesting different mechanisms of **TIMP-1 [?]** regulation of apoptosis depending on cell types.

Taken together, the present study unveils some of the mechanisms mediating the anti-apoptotic effects of **TIMP-1 [?]** in human **breast epithelial cells** through TIMP-1-specific signal transduction pathways.

Multivariate analysis disclosed that **TIMP1** overexpression in cancer cells was an independent determining factor for **prognosis** (p=0.006); TIMP1 overexpression in malignant cells appeared to correlate with favorable outcome, particularly in patients with lack of nodal metastases and in patients with MMP2-negative immunophenotype (p=0.0252).

Elevated serum concentrations of ICTP (>5 microg/liter) and/or **TIMP-1 [?]** (>300 ng/ml) correlated with poor **prognosis**.

In patients with advanced colorectal **cancer**, high levels of either gelatinase B or **TIMP [?]** complex were associated with shortened survival.

These observations suggest that **breast adenocarcinoma** MCF-7 cells in culture produce both soluble and membrane-bound factor(s) which stimulate the production of pro-MMPs and **TIMP-1** in neighbouring stromal cells, but the factor(s) released into the medium and that associated with **cell membranes** are probably different.

The selective induction of **TIMP-1** by OM may be influential in altering matrix destruction in chronic inflammation and **tumor** metastasis.

Differential regulation of **gelatinase A** and B and **TIMP-1 [?]** and -2 by TNFalpha and HIV virions in **astrocytes**.

In comparison with the control group, the postoperative serum concentrations of **TIMP-1 [?]** of the burned patients were significantly higher ($p < 0.05$) at any time and correlated with the total body surface area burned at the third and seventh postoperative days ($p < 0.05$; $r2 = 0.46$ versus $r2 = 0.53$) and the **Burn Scar** Index after 6 months ($p < 0.05$; $r2 = 0.65$).

Taken together, it was found that **arecoline** acted not only as an inhibitor on gelatinolytic activity of **MMP-2**, but also a stimulator for **TIMP-1 [?]** activity.

TIMP1 expression levels varied more widely in hybrids retaining an inactive X than in those with an active **X chromosome**, suggesting variable retention of the epigenetic silencing mechanisms associated with X inactivation.

top

Therefore, we investigated the contribution of methylation at the promoter to expression level variation and found that methylation of the **TIMP1** promoter correlated with instability and low level expression, whereas stable TIMP1expression from the inactive X equivalent to that seen from the active **X chromosome** was observed when the promoter was unmethylated.

Variability of **X chromosome** inactivation: effect on levels of **TIMP1** **RNA** and role of DNA methylation.

Neutrophils are first-line defense **leukocytes** and do not produce **gelatinase A** or **TIMP**.

To investigate the role of P. aeruginosa virulence factors in the repair of human airway **epithelial cells** (HAEC) in culture, we evaluated the effect of stationary-phase supernatants from the wild-type strain PAO1 on cell migration, **actin** **cytoskeleton** distribution, epithelial integrity during and after repair of induced wounds, and the balance between matrix metalloproteinases (MMP) and their tissue inhibitors (**TIMP**).

The **neutrophil** derived oxidant HOCl, but not the derived oxidant N-chlorotaurine, can inactivate **TIMP-1 [?]** at concentrations achieved at sites of inflammation.

Low levels of **indomethacin** (10(-7) M) significantly increased the production of **TIMP-1** by chondrocytes.

We have used a series of **somatic cell hybrids** segregating translocation and deletion **X chromosomes** to map the **TIMP [?]** gene on the human **X chromosome**.

These data indicate that **neutrophils** which infiltrate tissues in various inflammatory conditions may play an important role in regulating **TIMP [?]** activity in vivo through the action of **neutrophil** **elastase**.

Divergent effects of i on MMP and **TIMP** secretion from **monocytes** may be important in influencing matrix degradation in vivo.

The activation of proMMP-9 was increased to a greater extent with **plasmin** treatment than without **plasmin** in HFH-T2 and HepG2-HBV cells but the addition of recombinant **TIMP-1 [?]** inhibited the activation of proMMP-9.

This study demonstrates the potential role of **TIMP-1 [?]** as a target in gene therapy for **pancreatic cancer**.

METHODS: A poorly differentiated human **pancreatic cancer** cell line (PANC-1) underwent gene **transfection** to overexpress **TIMP-1 [?]** (CD-1 cells).

TNFalpha's effects on MMP and **TIMP [?]** expression were completely blocked by only one **PKC** inhibitor.

The aim of this study was to investigate the effect of **TIMP** **gene therapy** on human **pancreatic cancer**.

We therefore conclude that MS is associated with elevated levels of MMP and **TIMP** expressing blood **monocytes** that may contribute to MS pathogenesis.

The simultaneous deficiency of **TIMP-1 [?]** and -2 in endometriotic tissue suppose an additional proteinase inhibitor imbalance in **endometriosis**.

The **sensitivity** results of serum **laminin** and **TIMP-1 [?]** were 11% and 56% respectively.

Clinical usefulness of serum tissue inhibitor of metalloproteinases (TIMP)-2 assay in patients with chronic **liver disease** in comparison with serum **TIMP-1 [?]**.

The high level of **TIMP-1 [?]** appeared to be related to malignant phenotype in **ovaries** as well as the high level of MMP-9.

TIMP is much more efficient in human explants, indicating the limited participation of human **plasmin** in the degradation of human cartilage.

top

ECM degradation was completely blocked (P < 0.001) by two **plasmin** inhibitors, **alpha-2-antiplasmin** (40 micrograms/ml) and **aprotinin** (216 KIU/ml), and partially reduced (-33 +/- 1.8%, P < 0.01) by **TIMP-1** (40 micrograms/ml), a specific inhibitor of matrix metalloproteinases.

Oligonucleotides to the reported sequence of human tumor cell **TIMP-1** were used for reverse-transcriptase **PCR** to generate a 700 bp clone of the 28 kDa inhibitor from **keratoconus** keratocyte cytoplasmic **RNA**.

TIMP [?] cDNAs were quantitated by competitive **polymerase chain reaction** assays.

Regulation of **TIMP-1 [?]** phenotypic expression in Epstein--Barr virus-immortalized **B lymphocytes**.

The purpose of this study was to investigate the effects of SI-27 on MMP- 1, -2, -3, -9, and **TIMP-1 [?]**, -2 secreted by human **glioma** cell lines (U87MG, U251MG, U373MG, and Y98G).

TIMP-1 [?] values detect cirrhosis with 100% **sensitivity** but only 56% and 75% **specificity**.

Plasma **TIMP-1 [?]** values detect fibrosis with a **sensitivity** of 52% and 67% and a **specificity** of 68% and 88% resulting in overall efficiency rates of 68% and 71%, respectively.

The relationship between urinary **TIMP-1 [?]**, muscle-invasion, and **disease progression** in **bladder cancer** is at variance with its role as an inhibitor of MMPs and warrants additional evaluation.

It was previously demonstrated that **TIMP-1 [?]** inhibits apoptosis in germinal center **B cells** and induces further differentiation.

CONCLUSIONS: Our results indicated that ICTP and **TIMP-1 [?]** are good prognostic markers in **lung cancer**.

MMP and **TIMP** expression in head and neck **squamous cell carcinomas** was determined by quantitative **reverse transcriptase polymerase chain reaction** (qRT-PCR). qRT-PCR allows measurement of several mRNAs from as little as 4 &mgr;g of total cellular RNA.

We propose that **TIMP-1 [?]** acts as a survival factor controlling **B-cell** growth and apoptosis through an autocrine regulation process involving **IL-10** secreted by EBV-B lymphocytes.

In patients with **gastric cancer**, plasma **TIMP-1 [?]** seem to be an independent and most powerful prognosticator for the survival.

The correlation between the increased **TIMP-1 [?]** expression and cancer stage noted in this study reflects a role of **TIMP-1** in predicting

the aggressive behavior of **gastric cancer**.

The effects of **dibutyryl cyclic AMP** (DBcAMP) on tissue inhibitor metalloproteinase (**TIMP**) expression were studied in the human **hepatoma** cell line PLC/PRF/5 with relation to the invasive activity of the cells.

Measurement of matrix metalloproteinases (MMPs) and tissue inhibitor of metalloproteinases-1 (**TIMP-1 [?]**) in patients with **knee osteoarthritis**: comparison with generalized **osteoarthritis**.

Metalloproteinases and tissue inhibitor of metalloproteinase 1 (**TIMP-1 [?]**) in endometrial flushings from pre- and post-menopausal women and from women with endometrial **adenocarcinoma**.

MMPs and their inhibitors are present in most cervical **adenocarcinomas**, independent of tumor grade or subtype, but with the exception of **TIMP-1 [?]**, they are not expressed in nonneoplastic endocervical epithelium.

In **periodontitis**, **TIMP-1** and -2 mRNA-expressing cells showed significantly different localization.

Tissue inhibitor of metalloproteinases (**TIMP**) 1, 2 and 3 are related **proteins** that can form complexes with all known matrix metalloproteinases (MMPs).

top

Astrocytomas had low gelatinolytic activity and the tumor cells showed no immunoreactivity for MMP's and **TIMP-1**.

Glioblastomas, **anaplastic astrocytomas**, and metastatic tumors showed high gelatinolytic activity and positive immunostaining for MMP's; **TIMP-1** was also expressed in these tumors, but some tumor cells were negative for the antibody.

BACKGROUND: In an attempt to identify the factor(s) involved in the modulation of the degradative pathway of **articular cartilage**, we previously reported a possible imbalance between the levels of biologically active forms of metalloproteases and tissue inhibitor of metalloprotease (**TIMP [?]**) in **osteoarthritis** (OA) cartilage.

The MMP-2/TIMP-2 ratio increased as tumor invasion and metastasis progressed, suggesting that an imbalance in the MMP and **TIMP [?]** ratio promote the invasion and metastasis of **bladder cancers**.

CONCLUSIONS: These results provide the first clinical evidence suggesting that **TIMP-1 [?]** could promote growth of Hodgkin's lymphoma, and may be linked to **connective tissue** turnover in the nodular sclerosis subtype.

Results from these studies suggest that **TIMP-1 [?]** enhances tumorgenicity by potentiating **keratinocyte** hyperproliferation and appearance of chromosomal aberrations in premalignant cells, thereby increasing their risk to undergo malignant conversion.

BACKGROUND AND OBJECTIVE: Persistent **asthma** symptoms are associated with airway inflammation and remodeling, which may be mediated through metalloproteinase (MMP) and tissue inhibitor of metalloproteinase (**TIMP**).

The aim of this study was to evaluate MMPs and **TIMP** involvement in **toluene diisocyanate** (TDI)-induced **asthma**.

In Grade 1 **carcinomas** **TIMP-1** was predominantly immunolocalized to the stromal compartment with variable tumor cell localization being observed in Grades 2 and 3 **carcinomas**.

Stromal cells expressed transcripts of both **TIMP-1 [?]** and -2.

We previously reported an elevated serum **TIMP-1 [?]** level in patients with **systemic sclerosis** (SSc).

Elevation of serum and urine levels of **TIMP-1 [?]** and **tenascin** in patients with renal disease.

CONCLUSION: Urinary concentrations of **tenascin** and **TIMP-1 [?]** are elevated in association with renal disease and may reflect specific aspects of renal fibrosis.

MMP and **TIMP** are thus mainly synthesised by cancer cells in effusions, while **stromal cells** have a similar role in solid tumours.

Induction of pro-MMP-9 and reduction of **TIMP** expression did not require cell-cell contact and were mediated by a soluble factor(s) present in the **conditioned medium** of the effector cell.

Basal production of **TIMP-1 [?]** by **cultured cells** was not different between PCOS and normal groups.

Conversely, the diffuse positive rate of **TIMP-1 [?]** was higher in the benign and borderline ovarian tumors than that in **ovarian carcinomas**.

BACKGROUND: The serum tissue inhibitor of metalloproteinases 1 (**TIMP-1 [?]**) level was reported to be a useful indicator of disease activity, especially of lung fibrosis in patients with **systemic sclerosis**.

TIMP-1 [?] may potentially contribute to the pathogenesis of increased submucosal extracellular matrix deposition in **asthma**.

EXPERIMENTAL DATA: MMP and **TIMP [?]** expression is well studied in a variety of **kidney** disorders, particularly in **diabetes mellitus** and in experimental glomerulonephritis.

top

Taken together, these data suggest that: 1) a balance between MMPs and TIMPs has an important role to play in human **brain tumors**; 2) **TIMP** expression may be valuable markers for tumor malignancy.

The changes in ECM and the localization of matrix metalloproteinases (MMPs) and a tissue inhibitor of metalloproteinases (**TIMP**) in the lung tissues of patients with **bronchiolitis obliterans organizing pneumonia** (**BOOP**) and idiopathic **pulmonary fibrosis** (IPF) were investigated.

These results showed that secretion of MMPs and **TIMP-1 [?]** is regulated by normal tissues and peritoneum provides the best conditions for **ovarian cancer** cell invasion.

Addition of **conditioned medium** from these normal tissues to NOM1 cells increased the levels of MMPs and **TIMP-1 [?]** in NOM1 **conditioned medium**.

Isolated stellate cells expressed **TIMP-1** and -2 **RNA**.

Expression of matrix metalloproteinases and their inhibitor **TIMP-1 [?]** in the rat **carotid artery** after balloon **injury**.

The presence of **TIMP-1** in **cultured cells** was also detected immunocytochemically.

Positive **TIMP-1 [?]** staining was identified in osteoblasts/osteocytes and endothelial cells of all specimens, and in the lining **epithelium** and subepithelial fibrous **connective tissue** wall of five **radicular cysts** with an intense inflammatory cell infiltrate.

The authors conducted a comparison study of matrix metalloproteinase (MMP) and tissue inhibitor of metalloproteinase-1 (**TIMP-1**) activities in clinically different metastatic types of **ovarian cancer**, **cervical**

cancer, and **endometrial cancer** tissues.

The role of matrix metalloproteinases (MMP's) and their inhibitor, tissue inhibitor of metalloproteinases-1 (**TIMP-1**), in human **brain tumor** invasion was investigated.

However, a relative decline in the detectable **TIMP [?]** levels in **keratoconus** cultures resulted in an apparent three-fold increase in the ratio of MMP-2/TIMP.

Result page: **1** 2 **[Next]**